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Sex-specific characteristics associated with the elevated triglyceride to high-density lipoprotein cholesterol ratio in a population-based study

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ABSTRACT

Aims: Evidence suggests that changes in the ratio of triglycerides to HDL-c (TG/HDL-c) predict metabolic and cardiovascular diseases, but the factors that might be associated with TG/HDL-c and whether they would be different between men and women are still unknown. We aimed to identify the sex-specific variables associated with TG/HDL-c in adults.

Methods: This cross-sectional population-based study investigated 1603 adults not taking lipid-lowering medication. Sociodemographic characteristics were obtained in a home interview. Blood lipids were measured in participants instructed to fast for at least 10 h. Anthropometric parameters were obtained using standard methods.

Results: TG/HDL-c increases in men towards the higher educational categories, while in women, it decreases in those with a higher educational level. Additionally, TG/HDL-c was higher in the highest socioeconomic class in men but lower in women. In men, age, overweight/obesity, sedentary behavior, and those with higher educational levels were independently associated with high TG/HDL-c (4th quartile). In women, however, overweight/obesity, hypertension, diabetes and tobacco smoking were associated with higher TG/HDL-c, while brown and black women presented lower chances of having a high TG/HDL-c than that of white women.

Conclusions: Men and women have different characteristics that are associated with a higher TG/HDL-c, highlighting the need for individualized approaches for preventing cardiometabolic diseases based on sex-specific differences in the TG/HDL-c.

1. Introduction

During the last decades in which the epidemiological transition has taken place in almost the entire world, chronic diseases have become a major public health issue in developing countries (Kelly et al., 2012). Technological advances associated with a fast-food-based diet contributed to the emergence of several risk factors of increasing incidence that predicts the development of cardiovascular and metabolic diseases (Ribeiro et al., 2016). These factors, such as obesity, sedentary lifestyle, unhealthy dietary patterns, and smoking habit, are well-known predictors of hypertension and type-2 diabetes, increasing the risk of cardiovascular and metabolic morbidity and mortality (Joseph et al., 2017).

One of the major risk factors for cardiometabolic diseases is dyslipidemia. Dyslipidemia is a metabolic disorder ensuing from an interaction of genetic background with environmental and sociodemographic factors characterized by increased levels of low-density lipoprotein cholesterol (LDL-c) and/or increased levels of triglycerides (TGs) and reduced levels of high-density lipoprotein cholesterol (HDL-c) (Parhofer, 2017). For instance, TGs are lipids produced to store energy for use in the fasting period, while HDL-c transports fat cholesterol from the body to the liver for excretion or reutilization. However,

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elevated TG and low HDL-C levels are classical predictors of insulin resistance and metabolic syndrome, two conditions strongly associated with coronary heart diseases (Morrison and Hokanson, 2009; Papageorgiou et al., 2016).

The ratio between TG and HDL-c (TG/HDL-c) is used as an indicator of dyslipidemia due to its association with increases in cardiovascular risk. Therefore, there has been a growing body of evidence describing the role of the TG/HDL-c ratio as a reliable surrogate marker for metabolic and cardiovascular diseases (Giannini et al., 2011; Masson et al., 2016). McLaughlin et al. (2003) showed that the TG/HDL-c ratio is a simple predictor of insulin resistance in a Caucasian population. An increased TG/HDL-c ratio indicates the presence of small dense LDL particles with strong atherogenic properties (Maruyama et al., 2003). In fact, it has been reported that the TG/HDL-c ratio is associated with increased atherosclerotic cardiovascular disease as well as overall mortality (Hadaegh et al., 2009). The association between the TG/HDL-c ratio and coronary artery disease has been demonstrated in the Brazilian population by Bertoluci et al. (2010), showing a great predictive value independent of age, sex, body mass index (BMI), diabetes mellitus and systolic blood pressure (SBP).

In Brazil, there are no population-based studies that have identified sex-specific variables associated with the increased TG/HDL-c ratio in the adult general population. Thus, our aim was to identify the clinical, anthropometric and sociodemographic characteristics that are associated with the high TG/HDL-c ratio in adults not taking lipid-lowering drugs and to test the hypothesis that determinants of high TG/HDL-c would have a sex-specific pattern.

2. Subjects, materials and methods

2.1. Study population

The present study represents a cross-sectional view of a population-based study that investigated the urban adult population of Vitória, Brazil. The study was conducted according to the MONICA-WHO Project guidelines, and detailed information on the design and sampling have been published elsewhere (Rodrigues et al., 2009, 2012). The final sample comprises 1662 individuals, from 25 to 64 years old, selected based on a multistage probability sampling plan. A total of 2268 residential homes located in Vitória were selected. The sampling plan seeks good representativeness in the socioeconomic, geographic and demographic aspects of city residents. The survey was conducted with just one resident of each selected home within the age group of the study. The participant selected at each home was given an explanation of the purposes of the research and invited to participate in the study after obtaining his or her consent. After that, they were invited to attend the University Hospital for clinical and laboratory examination on a single prescheduled day in the morning period. The project was approved by the institutional ethics committee, and all participants gave written informed consent.

2.2. Blood biochemical evaluation

For blood biochemical investigation, participants were instructed to fast for at least 10 h before the exams. The blood samples were drawn after venipuncture in the upper limb, performed by a previously trained laboratory technician. The samples were sent to a central laboratory (SESI-Vitória) for biochemical analysis using commercially available kits. The fasting glucose level was measured from blood collected in a tube containing fluoride as an anticoagulant. Diabetes was established if fasting blood glucose ≥ 126 mg/dL or by reporting the current use of oral hypoglycemic medication or insulin. For the lipid dosage, the anticoagulant used was ethylenediamine tetra-acetic acid. The LDL-c fraction was calculated indirectly using the Friedewald equation for triglycerides < 400 mg/dL. For the purpose of the present study, we removed those individuals who used any lipid-lowering medication (48 individuals).

2.3. Clinical and anthropometric assessment

Blood pressure was measured in fasting individuals, in the left arm using a mercury column sphygmomanometer, kept in the sitting position after a rest period of 5–10 min. The first and fifth Korotkoff phases were used to indicate systolic (SBP) and diastolic (DBP) blood pressure, respectively. The heart rate was calculated by counting pulse beating for 30 s. Hypertension was considered as SBP ≥ 140 or diastolic blood pressure DBP ≥ 90 mmHg or the use of any blood pressure-lowering drug.

Anthropometric parameters were obtained using standard methods (Rodrigues et al., 2010) and were collected by trained technicians. Body weight was obtained on a calibrated scale with an accuracy of 0.1 kg. Height was measured on a wall stadiometer with an accuracy of 0.5 cm. The body mass index (BMI) was measured as the ratio of body weight (kg) to height squared (m^2). Individuals were characterized as overweight and obese when BMI was between 25.0 and 29.9 kg/m^2 or ≥ 30.0 kg/m^2, respectively. Waist circumference (WC) was measured at the midpoint between the last costal arch and the iliac crest, considering the maximum point of normal expiration, with the individual in the standing position. The hip circumference was measured with an accuracy of 0.1 cm around the thighs, at the height of the greater trochanter, with the individual standing. Participants were considered normal when WC was < 94 for men and < 80 for women (Lean et al., 1995; Organization, 2008).

Data on physical activity and smoking habits were acquired using questionnaires. Individuals were considered sedentary if they did not report practicing sports or were not engaged in physical activity for leisure lasting at least 30 min per day for at least three days a week.

Smoking habits were investigated during the home interview, and subjects were classified as smokers, never smokers and past smokers. For the purpose of the present analysis, the last two groups were merged into nonsmokers. Individuals who reported the use of tobacco on a regular or occasional basis and those who reported having stopped smoking 6 months prior to the day of the interview were considered smokers.

2.4. Sociodemographic characteristics

In order to obtain the socioeconomic status, individuals were classified into one of 5 levels (A, B, C, D and E) according to a score obtained by a questionnaire filled in during the home visit. The A stratum represents the highest social class and the E the lowest one. In view of the small number of subjects in class E, classes D and E were combined for the purpose of this study. The construction of the score took into consideration the educational level and the number of consumer goods available at home (television, refrigerator, freezer, automobile, etc.). The educational level of participants was classified into 3 categories according to the number of years of school attended: high (completed higher education or higher certified technicians: ≥ 12 years), intermediate (completed high school: 8–12 years), and low (elementary school level or lower: < 8 years).

Ethnic-racial stratification was based on phenotypic parameters and based on self-report of participants regarding their ancestors. Thus, they were divided into the following ethnic-racial groups: white, black, and brown. Due to the small representativeness in this population, Native Americans and Asians were excluded from these analyses.

2.5. Statistical analyses

Statistical analyses were performed using the statistical package SPSS v.22 (Chicago, IL, USA). Data are presented as the mean ± standard deviation for continuous variables or as a frequency and percentage for dichotomous variables. The overall adequacy for the

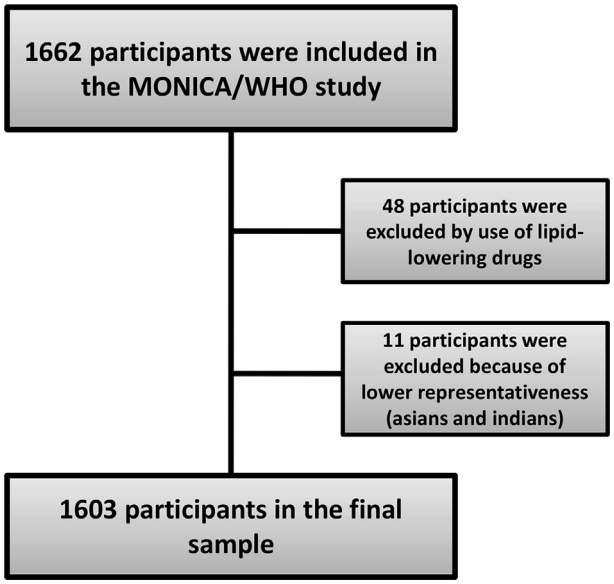

Fig. 1. Flowchart showing the structure of the final sample.

Gaussian distribution was assessed by the Kolmogorov-Smirnov test. Student's *t*-test or analysis of variance (ANOVA) with Tukey's post hoc test (in case of a significant F test) was used to evaluate differences between two or more means, respectively. Proportions were compared by using the Chi-squared test. Sex-specific quartiles of TG/HDL-c were used to distinguish between those with normal or elevated values (Fan et al., 2019). The association between categorized TG/HDL-c and its determinants was evaluated through crude and adjusted logistic regression based on an exploratory multiple logistic regression controlled for all variables included in the model and showed in the table. The statistical significance was set at $P < 0.05$ for proportions and means.

3. Results

After exclusion of participants taking lipid-lowering medication (n = 48) or participants with lower representativeness in the sample (Asians and Indians, n = 11), the final sample consisted of 1603 participants (45.7% were men) with a mean age of 44.5 ± 10.7 years (Fig. 1). The clinical and anthropometric characteristics of the study participants are shown in Table 1. Men had higher body weight, WC, WHR, and both SBP and DBP than those of women. However, BMI was higher in women than that in men. Only a few differences were noted between the sexes regarding blood biochemistry parameters (Table 1). For instance, uric acid and TG were higher in men than those in women. On the other hand, HDL-c levels were higher in women than the levels in men. Based on the individual values of TG and HDL-c, the TG/HDL-c ratio was higher in men than that in women as expected (3.72 ± 2.67 *vs* 2.61 ± 2.23, $P < 0.001$).

Supplementary Table S1 shows the mean value for the TG/HDL-c ratio stratified by clinical, anthropometric and sociodemographic characteristics. The TG/HDL-c ratio increases progressively with age in women but not in men. Nevertheless, the TG/HDL-c ratio increases with BMI and WC, regardless of sex. Neither physical activity nor tobacco smoking changed the TG/HDL-c ratio in men, but it increased in women with smoking habits. Interestingly, both socioeconomic status and educational level have different patterns concerning the TG/HDL-c ratio according to sex. In men, the TG/HDL-c ratio increases towards higher educational categories, while in women, it decreases in those with higher educational levels. Additionally, the same pattern was observed for socioeconomic status in which the TG/HDL-c ratio was higher in men in the highest socioeconomic class, while it was lower for women in the highest socioeconomic class.

Table 1
General characteristics of the sample stratified by sex.

	MEN (n = 728)	WOMEN (n = 875)	*P* value	ALL (n = 1603)
Age (years)	44.4 ± 10.8	44.5 ± 10.7	1.000	44.5 ± 10.7
Weight (kg)	74.3 ± 13.1	65.4 ± 14.4	< 0.001	69.5 ± 14.5
Height (cm)	169.3 ± 7.1	156.8 ± 6.2	< 0.001	162.5 ± 9.1
BMI (kg/m^2)	25.9 ± 3.9	26.6 ± 5.5	0.004	26.2 ± 4.9
WC (cm)	89.0 ± 10.9	83.5 ± 12.9	< 0.001	86.1 ± 12.3
WHR	0.92 ± 0.07	0.84 ± 0.08	< 0.001	0.87 ± 0.08
Uric acid (mg/dL)	5.48 ± 1.42	4.19 ± 1.31	< 0.001	4.78 ± 1.51
Glucose (mg/dL)	105.1 ± 27.2	103.3 ± 32.8	0.232	104.1 ± 30.3
Cholesterol (mg/dL)	211.7 ± 44.0	214.6 ± 44.7	0.554	213.3 ± 44.4
HDL-c (mg/dL)	42.3 ± 12.3	48.0 ± 12.0	< 0.001	45.4 ± 12.4
LDL-c (mg/dL)	140.1 ± 38.6	143.5 ± 39.3	0.112	141.9 ± 39.0
Non-HDL-c (mg/dL)	168.1 ± 43.2	165.7 ± 44.2	0.272	166.8 ± 43.8
TG (mg/dL)	152.0 ± 102.9	117.3 ± 83.1	< 0.001	133.1 ± 94.2
TG/HDL-c	3.72 ± 2.67	2.61 ± 2.23	< 0.001	3.11 ± 2.49
LDL-c/HDL-c	3.53 ± 1.27	3.21 ± 1.75	< 0.001	3.35 ± 1.56
SBP (mmHg)	130.1 ± 19.7	125.8 ± 23.3	< 0.001	84.3 ± 14.1
DBP (mmHg)	87.1 ± 13.9	81.9 ± 13.8	< 0.001	127.7 ± 21.8
HR (bpm)	68.7 ± 10.2	72.2 ± 11.4	< 0.001	70.8 ± 11.1
Hypertension (%)	354 (47.0%)	328 (37.3%)	< 0.001	682 (42.2%)
Diabetes (%)	55 (7.4%)	68 (7.7%)	0.900	123 (7.6%)
Overweight/Obesity (%)	418 (56.6%)	475 (54.4%)	0.328	893 (55.3%)

Data are shown as mean ± standard deviation. BMI, body mass index; WC, waist circumference; WRH, waist-to-hip ratio; HDL-c, high density lipoprotein cholesterol; LDL-c, low density lipoprotein cholesterol; TG, triglycerides; TG/HDL-c, TG to HDL-c ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

When the participants were allocated into sex-specific quartiles of the TG/HDL-c ratio, several clinical, anthropometric and sociodemographic characteristics changed proportionally. As observed in Table 2, all variables changed significantly over the quartile distribution, except height, HR, physical activity status and tobacco smoking in men and height, HR and physical activity in women. It is important to note that TG increases approximately 4-fold, while HDL-c decreases 1.3-fold from the lowest quartile to the highest quartile, regardless of sex (Fig. 2).

We next dichotomized the TG/HDL-c ratio into two categories: normal (1st, 2nd and 3rd quartiles) and increased (4th quartile). Based on the quartile distribution, the cutoff for the increased TG/HDL-c ratio was > 4.81 for men and > 3.23 for women. Based on that classification, we performed a multiple logistic regression to identify the sex-specific characteristics that are independently associated with an increased TG/HDL-c ratio. In men, age, overweight/obesity, sedentary behavior, and those with higher educational levels were independently associated with a high TG/HDL-c ratio (Table 3). In women, however, overweight/obesity, hypertension, diabetes and tobacco smoking were associated with a higher TG/HDL-c ratio, while brown and black women presented lower chances of having a high TG/HDL-c ratio than white women (Table 3).

Based on the lower number of diabetic participants, we performed multiple logistic regression after excluding those participants. Even with a few changes in the odds ratio, the results remained unchanged based on their statistical significance (data not shown).

4. Discussion

Previous studies have shown that an increased TG/HDL-c ratio is one of the major risk factors for cardiovascular diseases, insulin resistance and metabolic syndrome (Gonzalez-Chavez et al., 2011;

Table 2
Clinical, anthropometric and sociodemographic characteristics divided by sex-specific quartiles of TG/HDL-c ratio.

	MEN (n = 728)					WOMEN (n = 875)				
	TG/HDL-c ratio					TG/HDL-c ratio				
	Q1 (< 1.74)	Q2 (1.74–2.93)	Q3 (2.94–4.81)	Q4 (> 4.81)	*P* value	Q1 (< 1.27)	Q2 (1.27–2.00)	Q3 (2.01–3.23)	Q4 (> 3.23)	*P* value
Age (years)	41.8 ± 11.5	43.6 ± 10.9	45.9 ± 10.5	46.0 ± 10.1	< 0.001	41.4 ± 9.6	42.9 ± 10.4	46.7 ± 10.5	47.1 ± 11.1	< 0.001
Weight (kg)	68.9 ± 13.2	71.8 ± 11.8	75.9 ± 11.3	80.2 ± 13.1	< 0.001	59.2 ± 12.0	64.2 ± 14.1	67.2 ± 15.2	71.2 ± 13.3	< 0.001
Height (cm)	169.4 ± 7.5	169.5 ± 6.9	169.5 ± 7.7	169.0 ± 6.4	0.922	157.1 ± 5.9	157.5 ± 6.7	156.6 ± 5.9	156.2 ± 6.0	0.102
BMI (kg/m^2)	23.9 ± 3.9	24.9 ± 3.5	26.4 ± 3.1	28.0 ± 3.9	< 0.001	23.9 ± 4.3	25.8 ± 5.4	27.4 ± 5.8	29.2 ± 4.9	< 0.001
WC (cm)	83.0 ± 10.6	86.3 ± 9.7	91.5 ± 9.2	94.8 ± 9.8	< 0.001	76.7 ± 10.6	81.5 ± 12.8	85.8 ± 12.7	90.2 ± 11.2	< 0.001
WHR	0.88 ± 0.06	0.90 ± 0.06	0.93 ± 0.06	0.95 ± 0.06	< 0.001	0.80 ± 0.07	0.82 ± 0.08	0.85 ± 0.07	0.88 ± 0.08	< 0.001
Uric acid (mg/dL)	4.94 ± 1.27	5.25 ± 1.24	5.60 ± 1.53	6.18 ± 1.35	< 0.001	3.77 ± 1.04	3.90 ± 1.14	4.27 ± 1.22	4.80 ± 1.46	< 0.001
Glucose (mg/dL)	98.7 ± 23.9	102.8 ± 23.3	108.5 ± 34.0	109.2 ± 26.4	0.001	93.8 ± 12.9	98.0 ± 14.	103.5 ± 28.2	116.0 ± 51.5	< 0.001
Cholesterol (mg/dL)	195.2 ± 40.7	201.5 ± 37.7	221.2 ± 43.9	223.5 ± 44.9	< 0.001	199.4 ± 39.0	205.7 ± 38.5	220.0 ± 41.6	232.7 ± 48.2	< 0.001
HDL-c (mg/dL)	53.1 ± 16.2	42.4 ± 7.4	40.1 ± 7.8	33.9 ± 6.9	< 0.001	57.5 ± 13.4	49.6 ± 9.2	45.8 ± 8.4	38.9 ± 7.9	< 0.001
LDL-c (mg/dL)	130.0 ± 34.7	139.4 ± 34.2	150.7 ± 40.9	140.2 ± 41.8	< 0.001	131.4 ± 34.8	140.1 ± 35.6	151.4 ± 38.4	153.1 ± 43.6	< 0.001
Non-HDL-c (mg/dL)	142.1 ± 36.0	159.1 ± 35.5	181.1 ± 41.9	189.6 ± 42.5	< 0.001	141.9 ± 35.7	156.0 ± 36.2	174.3 ± 39.3	193.7 ± 46.1	< 0.001
TG (mg/dL)	60.4 ± 16.4	98.2 ± 22.6	151.9 ± 34.5	248.6 ± 64.7	< 0.001	57.5 ± 15.6	79.5 ± 16.9	114.4 ± 23.6	203.3 ± 68.2	< 0.001
SBP (mmHg)	127.8 ± 20.6	126.6 ± 17.8	130.7 ± 17.3	133.2 ± 19.7	0.005	117.7 ± 18.9	120.8 ± 20.8	130.4 ± 24.8	133.3 ± 24.3	< 0.001
DBP (mmHg)	84.7 ± 14.0	84.0 ± 13.1	88.5 ± 12.5	89.0 ± 13.5	< 0.001	76.9 ± 12.4	79.5 ± 12.9	83.9 ± 13.8	86.8 ± 13.9	< 0.001
HR (bpm)	68.5 ± 8.9	67.1 ± 11.2	68.6 ± 12.1	69.8 ± 8.9	0.085	72.7 ± 10.7	70.5 ± 10.1	70.7 ± 9.6	75.4 ± 14.2	0.098
Hypertension (n, %)	66 (37.3)	75 (41.9)	89 (50.5)	98 (55.4)	< 0.001	43 (20.5)	50 (23.7)	101 (47.2)	121 (56.8)	< 0.001
Diabetes (n, %)	3 (1.7)	10 (5.6)	17 (9.6)	19 (10.7)	< 0.001	4 (1.9)	9 (4.3)	16 (7.5)	33 (15.5)	< 0.001
Physical Activity (n, %)	48 (28.2)	54 (30.8)	46 (26.7)	46 (26.4)	0.531	55 (26.2)	43 (20.4)	49 (22.9)	43 (20.2)	0.228
Tobacco smoking (n, %)	38 (22.6)	43 (25.0)	46 (26.6)	50 (28.6)	0.193	29 (14.3)	38 (18.5)	45 (21.4)	55 (26.2)	0.002
Educational level (n, %)	–	–	–	–	–	–	–	–	–	–
< 8	109 (28.2)	100 (25.9)	93 (24.1)	84 (21.8)	0.006	92 (19.0)	117 (24.2)	137 (28.4)	137 (28.4)	< 0.001
8 – 12	33 (19.4)	47 (27.6)	46 (27.1)	44 (25.9)	0.190	70 (30.6)	58 (25.3)	49 (21.4)	52 (22.7)	0.011
≥ 12	29 (20.7)	32 (22.8)	36 (25.8)	43 (30.7)	0.046	40 (33.1)	32 (26.4)	26 (21.5)	23 (19.0)	0.006
Socioeconomic status (n, %)	–	–	–	–	–	–	–	–	–	–
A	15 (19.7)	13 (17.1)	22 (28.9)	26 (34.2)	0.025	30 (37.0)	21 (25.9)	12 (14.8)	18 (22.2)	0.016
B	38 (19.9)	52 (27.2)	53 (27.7)	48 (25.1)	0.278	65 (27.8)	56 (23.9)	61 (26.1)	52 (22.2)	0.199
C	43 (20.9)	60 (29.1)	48 (23.3)	55 (26.7)	0.283	59 (22.1)	70 (26.2)	73 (27.3)	65 (24.3)	0.569
D + E	77 (33.2)	54 (23.3)	53 (22.8)	48 (20.7)	0.001	56 (21.0)	64 (24.1)	68 (25.6)	78 (29.3)	0.028
Race (n, %)	–	–	–	–	–	–	–	–	–	–
White	46 (18.5)	60 (24.1)	72 (28.9)	71 (28.5)	0.004	74 (26.0)	62 (21.8)	69 (24.3)	79 (27.8)	0.507
Mixed	98 (25.8)	96 (25.3)	93 (24.5)	93 (24.5)	0.379	117 (24.3)	129 (26.8)	120 (24.9)	116 (24.0)	0.639
Black	26 (41.3)	18 (28.6)	8 (12.7)	11 (17.4)	< 0.001	15 (24.6)	17 (27.9)	15 (24.6)	14 (22.9)	0.749

Data are shown as mean ± standard deviation. BMI, body mass index; WC, waist circumference; WRH, waist-to-hip ratio; HDL-c, high density lipoprotein cholesterol; LDL-c, low density lipoprotein cholesterol; TG, triglycerides; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

Wakabayashi, 2012; Eeg-Olofsson et al., 2014). Additionally, some authors consider that the TG/HDL-c ratio can better predict vascular health than either one does individually (TG or HDL-c) (de Giorgis et al., 2014). Thus, the TG/HDL-c ratio may represent a reliable tool to foresee cardiometabolic risk (Giannini et al., 2011). However, some information is still missing regarding the TG/HDL-c ratio. For instance, the distribution and association of the TG/HDL-c ratio with different strata of clinical, anthropometric and sociodemographic variables in Brazilians is unknown. Additionally, in most cases, authors do not present the results stratified by sex, which makes data interpretation

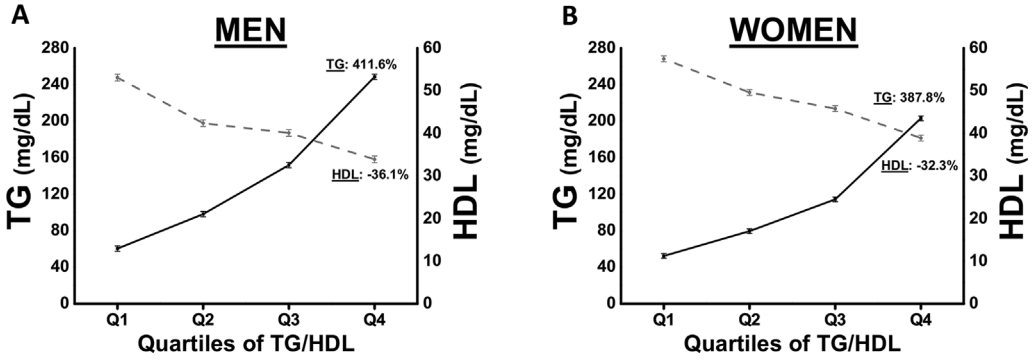

Fig. 2. Changes in TG and in HDL-c by TG/HDL-c ratio quartile distribution in men and women.

Table 3
Multiple logistic regression for the association between high levels of TG/HDL-c ratio and clinical, anthropometric and sociodemographic characteristics stratified by sex.

	MEN		WOMEN	
	Odds ratio (95% CI)		Odds ratio (95% CI)	
	Crude (n = 728)	Adjusted (n = 671)	Crude (n = 875)	Adjusted (n = 829)
Age (decades)				
25–34	1 (reference)	1 (reference)	1 (reference)	1 (reference)
35–44	2.09 (1.24–3.51)	**1.76 (1.01–3.08)**	1.32 (0.82–2.11)	1.12 (0.67–1.87)
45–54	2.30 (1.38–3.83)	**1.86 (1.06–3.27)**	1.42 (0.90–2.25)	0.87 (0.51–1.47)
55–64	1.99 (1.14–3.48)	1.51 (0.80–2.83)	2.73 (1.69–4.38)	1.26 (0.72–2.20)
Overweight/Obesity	3.66 (2.47–5.44)	**3.22 (2.10–4.92)**	4.70 (3.25–6.80)	**3.97 (2.66–5.92)**
Hypertension	1.61 (1.14–2.26)	1.27 (0.85–1.88)	2.99 (2.17–4.11)	**2.03 (1.38–2.99)**
Diabetes	1.99 (1.09–3.64)	1.51 (0.79–2.91)	3.83 (2.26–6.49)	**2.02 (1.14–3.62)**
Physical Activity	0.89 (0.61–1.32)	**0.65 (0.41–0.99)**	0.84 (0.57–1.23)	0.82 (0.53–1.26)
Tobacco smoking	1.21 (0.83–1.79)	1.29 (0.83–1.99)	1.27 (0.94–1.72)	**1.57 (1.13–2.16)**
Educational level				
< 8	1 (reference)	1 (reference)	1 (reference)	1 (reference)
8–12	1.40 (0.86–2.28)	1.42 (0.79–2.55)	1.37 (0.80–2.33)	1.60 (0.85–3.04)
≥ 12	1.76 (1.16–2.68)	**2.31 (1.20–4.42)**	1.85 (1.14–2.99)	1.51 (0.78–2.90)
Socioeconomic status				
A	1 (reference)	1 (reference)	1 (reference)	1 (reference)
B	0.65 (0.36–1.15)	0.83 (0.43–1.60)	1.00 (0.54–1.84)	1.25 (0.60–2.62)
C	0.70 (0.39–1.23)	1.38 (0.64–3.01)	1.12 (0.62–2.04)	1.32 (0.59–2.92)
D + E	0.50 (0.28–0.89)	1.12 (0.48–2.59)	1.45 (0.81–2.61)	1.19 (0.51–2.72)
Race				
White	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Mixed	0.81 (0.57–1.16)	0.88 (0.58–1.33)	0.87 (0.63–1.19)	**0.65 (0.45–0.95)**
Black	0.54 (0.27–1.09)	0.59 (0.27–1.28)	0.81 (0.43–1.35)	**0.49 (0.22–0.97)**

Data are presented as the OR (95% CI). TG/HDL-c was categorized into normal (Q1, Q2, and Q3) and elevated (Q4).

difficult because of the well-known effect of estrogens on HDL-c levels. Thus, we performed a population-based study to identify the sex-specific characteristics that are associated with a higher TG/HDL-c ratio in adults of an urban area of Brazil.

In our study, we confirmed the well-reported difference in the TG/HDL-c ratio between men and women (Weiss et al., 2015). In fact, it is already known that young women have a better lipid profile than men. This difference is expected for the TG/HDL-c ratio based on individual levels of TG and HDL-c between the sexes. Young women have higher levels of HDL-c than men, which slightly decrease during climacteric ages. Additionally, women present lower levels of TG than men (de Aloysio et al., 1999). Based on these data, it is expected that the ratio between TG and HDL-c would be lower in women than that in men. Thus, the cutoff point to identify cardiometabolic risk has been reported to be different for men and women (Salazar et al., 2011). Nevertheless, the expected normal value for men and women is established as < 3, based on the individual cutoff for TG (> 150 mg/dL) and HDL-c (< 50 mg/dL) (Xavier et al., 2013). However, this cutoff point was not tested for its prediction ability.

In this population-based study, we showed that the TG/HDL-c ratio increases with age, BMI and WC regardless of sex. As a ratio, it is easy to determine why the TG/HDL-c ratio increases with age once both TG and HDL-c alone are changed by age in the opposite direction (increase in TG levels and decrease in HDL-c levels) (Kannel et al., 1971). However, after controlling for confounders, the association between age and the TG/HDL-c ratio was found to be significant only for men. In fact, there are several risk factors that affect women from menopause on. However, our study population comprises individuals up to 64 years old. Thus, even though the crude OR in women in the highest age category was higher (OR: 2.73), it did not reach statistical significance when controlled for confounders. Accordingly, we can hypothesize that during menopause, other risk factors would be involved in increasing the TG/HDL-c ratio more effectively than age per se (Kannel et al., 1976).

Adiposity as shown by BMI and WC contributes to increases in TG levels in adults (van Wijk et al., 2003). Indeed, the association between the TG/HDL-c ratio and overweight/obesity was strong after adjustment for confounders, regardless of sex. These results corroborate previous studies in the general population showing a great association between adiposity markers and the TG/HDL-c ratio (Wakabayashi, 2012). Physical activity has also been reported to improve lipid profiles and control body weight in adults. In fact, the lipid profile improves with increases in the time spent engaged in physical activity and worsens with increased screen time (Crichton and Alkerwi, 2015). However, after controlling for confounders, the practice of physical activity was significantly associated with a lower TG/HDL-c ratio only in men.

Women in the highest quartile for the TG/HDL-c ratio were positively associated with diabetes and hypertension in our study. In fact, studies have shown that the TG/HDL-c ratio was an independent risk factor for type 2 diabetes and hypertension. A longitudinal study showed a strong association between the TG/HDL-c ratio and incident hypertension in women (Tohidi et al., 2012). These data highlight an excessive cardiovascular risk by combined risk factors as proposed by the Framingham Heart Study (Wilson et al., 1998). Despite the metabolic risk caused by the TG/HDL-c ratio, the association with diabetes and hypertension causes a major increase in the risk of coronary heart disease (Wilson et al., 1998). Indeed, according to da Luz et al. (da Luz et al., 2008), the TG/HDL-c ratio has been shown to be a predictor of coronary artery disease development and also to be related to the severity of vessel involvement.

Although some authors have reported an association between the TG/HDL-c ratio and metabolic parameters, there are only a few studies exploring other clinical, socioeconomic and educational and racial relationships. For instance, it was reported that the association between insulin resistance and the TG/HDL-c ratio is higher in whites than in blacks (Giannini et al., 2011). Our data showed that brown and black

women, but not men, have a lower chance of having a high TG/HDL-c ratio. Sumner et al. (2005) showed that the TG/HDL-c ratio is not a reliable predictor of insulin resistance in black Africans. Although the TG/HDL-c ratio in Caucasians and Koreans has shown a positive correlation with insulin resistance, such a correlation was not found in African Americans, indicating differences according to ethnicity. This sex-specific difference might be partially explained by the low level of TG in women and in blacks, helping to understand the fact that ethnicity was only associated with the TG/HDL-c ratio in women but not in men.

Many studies have indicated that the socioeconomic level represents an important cardiovascular risk factor, since it influences some health characteristics of individuals (Schultz et al., 2018). In this sense, inadequate eating habits such as a low intake of fruits and vegetables and high consumption of sugars and fats contribute to the appearance of several cardiovascular complications and risk factors such as hypertension and excess body fat (Mozaffarian, 2016). However, socioeconomic status was not independently associated with a higher TG/HDL-c ratio in our study. In fact, neither TG nor HDL-c were associated with socioeconomic status, unlike total cholesterol and LDL-c (Espírito-Santo et al., 2019). Additionally, socioeconomic status might maintain some collinearity with educational level as reported by others (Heiss et al., 1980; Benetou et al., 2000). In fact, higher educational categories were associated with the TG/HDL-c ratio regardless of sex. However, after controlling for confounders, a high educational level was significantly associated with higher levels of the TG/HDL-c ratio in men but not in women. These data might be explained by the sex-specific pattern of the lipid profile according to educational levels. In men, the prevalence of a higher TG/HDL-c ratio increases in those individuals attending $\geq$12 years of education, while it decreases in higher-educated women.

There are a few limitations to our study that cannot be ruled out. As a cross-sectional survey, we cannot establish any causality. A longitudinal study would be a better choice to establish causal associations between the TG/HDL-c ratio and clinical, anthropometric and sociodemographic characteristics. The fasting period was slightly lower (10 h instead of 12 h) than the recommendation for blood lipid analysis (Scartezini et al., 2017). Additionally, the use of estrogens or any type of hormonal replacement therapy was not considered as a confounding factor in this study.

5. Conclusions

In summary, we showed that men and women have different characteristics that are associated with a higher TG/HDL-c ratio. From all clinical, anthropometric, and sociodemographic characteristics tested, only overweight and obesity were significantly associated with TG/HDL-c in both men and women. Age, physical activity and educational level were associated with the TG/HDL-c ratio only in men, while hypertension, diabetes, smoking habit and race were found to be associated with TG/HDL-c exclusively in women. These results highlight the need for individualized approaches to preventing cardiometabolic diseases based on these sex-specific differences in the predictors of the TG/HDL-c ratio.

Author's contribution

LRES, TOF, NAA, LAX, GAM, MFS participated in the analysis and interpretation of data, and drafting the manuscript article; **JGM** participated to the conception and design, analysis and interpretation of data, and the final approval of the version to be published; **MPB** participated in the conception and design, analysis and interpretation of data, drafting of the article and critical revision for important intellectual content, and the final approval of the version to be published.

Declaration of competing interest

The authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.obmed.2019.100151.

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